ered to the bone marrow as compared with the liver. There was a linear relationship between the infused dose of Y-90 and the estimated radiation dose delivered to the BM. Mean absorbed radiation doses were: bone marrow 10.23 ± 1.8 cGy/MBq; liver 2.67 ± 2.0 cGy/MBq; spleen 7.10 ± 3.75 cGy/MBq. Total absorbed radiation doses at each Y-90 dose level are shown in Table 1. No additional toxicity due to the additional radiation was seen. Engraftment: neutrophils >0.5 by day +13.8 (range 11-22); platelets >50 by day +12.7 (range 10-22), no graft failures. In one patient with myeloma, focal uptake of radiolabelled antibody was seen at sites of disease activity suggesting in vivo targeting of myeloma. This is consistent with our finding of CD66 antigen expression by malignant plasma cells as shown by flow cytometry. There was a trend to greater disease response as the radiation dose increased, with a greater proportion of patients at the higher radiation dose levels achieving a CR. **Conclusions:** The radiolabelled anti-CD66 monoclonal antibody showed consistently excellent BM targeting and very low uptake by non-haematopoietic organs. Up to 30 Gy of radiation was delivered to the BM with no additional toxicity to other organs. Phase II studies are under way using the Y-90-labelled anti-CD66 in RIC-allogeneic SCT protocols and for autologous SCT for myeloma.

Table 1. *Organ Dosimetry*

Dose level (MBqkg)	Organ Dose in (Gy)		
	Bone Marrow	Liver	Spleen
5	4.1	1.4	1.1
10	9.1	1.3	2.4
25	15.6	3.7	12.6
37.5	25.0	7.4	5.1

GVH/GVL

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PREVENTION OF ACUTE GRAFT-VERSUS-HOST DISEASE DESPITE COMPENSATORY FUNCTION OF LYMPHOID ORGANS IN VIVO

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Acute graft-versus-host disease (aGVHD) results from alloreactive donor derived T cells attacking targets in the gastrointestinal tract, liver and skin. We observed the initiation and rapid kinetics of aGVHD in a murine model [FVB/N (H-2^q) into irradiated BALB/c (H-2^d)] using in vivo bioluminescence imaging. The transition from the initiation to the effector phase of aGVHD (day 3-4) was characterized by rapid T cell proliferation and upregulation of gut homing receptors α4β7, αEβ7 and CCR9 on alloreactive T cells in Peyer's patches (PP), mesenteric lymph nodes (LN) and spleen, but not peripheral LNs. Therefore we asked whether the lack of specific lymphoid priming sites would lead to decreased alloreactive T cell infiltration in the gut compared to the liver and skin. Using PP deficient mice, we observed that mesenteric LN and spleen compensate for the lack of PP as alloreactive priming sites. Transplantation of PP and LN deficient mice ($LT\alpha^{-/-}$) showed that the spleen alone was sufficient to cause the complete profile of aGVHD with a time course similar to that of wild-type mice. Splenectomized mice with intact secondary lymphoid organs also developed aGVHD. Strikingly, treatment of splenectomized recipients with blocking antibodies against the lymphoid homing receptors L-selectin and MAdCAM-1 prevented GVHD with 100% survival (>120 d, $P < .0001$). Our study shows that multiple priming sites are involved in GVHD initiation, the spleen compensating for the lack of PP and mesenteric LN, and vice versa. In contrast, splenectomy and antibody blocking resulted in a clear survival benefit for all recipients. A.B. and S.S. contributed equally to this study.

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THE HAPLOIMMUNOSTORM SYNDROME: A DISTINCT CLINICAL ENTITY SEEN IN HLA-HAPLOIDENTICAL CELLULAR IMMUNOTHERAPY

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An immune-mediated anti-tumor response is the ultimate goal of allogeneic transplantation for relapsed, refractory malignancies. We developed a transplant protocol with less toxicity compared with standard allogeneic transplantation. We utilized multiple donor lymphocyte infusions after nonmyeloablative HLA-haploidentical stem cell transplantation for refractory disease. We have performed a total of 41 HLA-mismatched transplants with escalation of the CD3+ dose to 2×10^8 cells/kg using G-CSF primed product, with a conditioning regimen of 100 cGy total body irradiation. Our phase I/II study had 26 with hematologic malignancies. This therapy results in loss of detectable macrochimerism. Despite this, 13 responses, six major, occurred outside of macrochimerism. We have observed a new infusion related clinical entity named haploimmunostorm (HIS), observed after infusion. This syndrome occurred in 26 out of 30 (87%) patients with a CD3+ dose more than 1×10^8 cells/kg. In the syndrome, a constellation of symptoms occurred, some with variable penetrance, in which hyperpyrexia and malaise were a constant feature occurring as early as 4 hrs after cell infusion (median of 14 hrs). A morbilliform rash was seen in 40% of patients. Biopsies revealed no evidence of hyperacute or acute GVHD. Diarrhea was present in a 20% of patients; biopsies taken also failed to show any evidence of GVHD. Transient elevations of liver enzymes occurred in 40% of the patients usually. Steroids were used successfully if the HIS syndrome lasted more than 72 hrs. We used a Bioplex machine and analyzed 17 separate cytokine levels serially in these patients beginning with pre-treatment levels. Cytokine level analysis showed up to a 90 fold increase in baseline cytokine levels with significant increases of at least 10 fold in IFN-γ, IL-10, IL-13, IL-2, IL-5, IL-6, IL-7, IL-8, MCP-1, and MIP-1β. This syndrome appears to be immunologically based and represents neither hyperacute nor acute GVHD. This syndrome is different than an engraftment syndrome reported in some patients undergoing autologous transplant. Engraftment syndrome occurs at time of engraftment, opposed to HIS in which may be a rejection syndrome. Engraftment syndrome is similar to HIS but deviates with presence of capillary leak and pulmonary infiltrates. In summary, we have observed a new clinical entity that was not previously seen and is a result of the donors having a relatively intact immune system at the time of cell infusion.

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STATISTICAL MODELLING FOR CLINICAL AND GENETIC RISK FACTORS FOR GvHD AND SURVIVAL IN A COHORT OF EUROPEAN HLA MATCHED SIBLING TRANSPLANTS

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A cohort of 244 HLA matched sibling transplants from 5 centres within Europe were typed for SNPs or microsatellites (IL-1Rα, IL-4, IL-6, IL-10, IFNγ, TNFα, TNFR11, and ste-